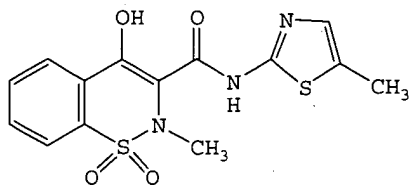


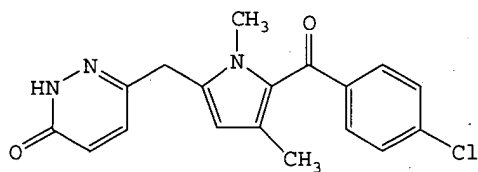
What Is Claimed Is:

1. A method for the treatment or prevention of Alzheimer's disease in a subject, the method comprising administering to the subject a cyclooxygenase-2 selective inhibitor or a pharmaceutically acceptable salt or prodrug thereof and an amyloid beta vaccine.  
5
2. The method of claim 1 wherein the cyclooxygenase-2 selective inhibitor comprises a chromene compound.  
10
3. The method of claim 2 wherein the chromene compound is a benzopyran or substituted benzopyran analog.
4. The method of claim 3 wherein the benzopyran or substituted benzopyran analog is selected from the group consisting of benzothiopyrans, dihydroquinolines and dihydronaphthalenes.  
15
5. The method of claim 1 wherein the cyclooxygenase-2 selective inhibitor comprises a tricyclic compound.  
20
6. The method of claim 5 wherein the tricyclic compound comprises a benzenesulfonamide or methylsulfonylbenzene.
7. The method of claim 1 wherein the cyclooxygenase-2 selective inhibitor comprises a phenyl acetic acid derivative.  
25
8. The method of claim 1 wherein the cyclooxygenase-2 selective inhibitor comprises:



or pharmaceutically acceptable salt or prodrug thereof.

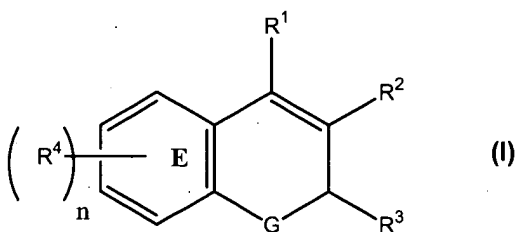
9. The method of claim 1 wherein the cyclooxygenase-2 selective inhibitor comprises:



or a pharmaceutically acceptable salt or prodrug thereof.

10

10. The method of claim 1 wherein the cyclooxygenase-2 selective inhibitor comprises a compound of the formula:



wherein n is an integer which is 0, 1, 2, 3 or 4;

wherein G is O, S or NR<sup>a</sup>;

wherein R<sup>a</sup> is alkyl;

- 15 wherein R<sup>1</sup> is selected from the group consisting of H and aryl;

wherein R<sup>2</sup> is selected from the group consisting of carboxyl, aminocarbonyl, alkylsulfonylaminocarbonyl and alkoxy carbonyl;

wherein R<sup>3</sup> is selected from the group consisting of haloalkyl, alkyl, aralkyl, cycloalkyl and aryl optionally substituted with one or more radicals selected from

- 20 alkylthio, nitro and alkylsulfonyl; and

wherein each  $R^4$  is independently selected from the group consisting of H, halo, alkyl, aralkyl, alkoxy, aryloxy, heteroaryloxy, aralkyloxy, heteroaralkyloxy, haloalkyl, haloalkoxy, alkylamino, arylamino, aralkylamino, heteroarylamino, heteroarylalkylamino, nitro, amino, aminosulfonyl, alkylaminosulfonyl, arylaminosulfonyl, heteroarylaminosulfonyl, aralkylaminosulfonyl, heteroaralkylaminosulfonyl, heterocyclosulfonyl, alkylsulfonyl, hydroxyarylcarbonyl, nitroaryl, optionally substituted aryl, optionally substituted heteroaryl, aralkylcarbonyl, heteroarylcarbonyl, arylcarbonyl, aminocarbonyl, and alkylcarbonyl;

wherein  $R^4$  together with the carbon atoms to which it is attached and the remainder of ring E forms a naphthyl radical;  
or a pharmaceutically acceptable salt or an isomer or a prodrug thereof.

11. The method of claim 10, wherein:

n is an integer which is 0, 1, 2, 3 or 4;

G is O, S or  $NR^b$ ;

$R^1$  is H;

$R^b$  is alkyl;

$R^2$  is selected from the group consisting of carboxyl, aminocarbonyl, alkylsulfonylaminocarbonyl and alkoxy carbonyl;

$R^3$  is selected from the group consisting of haloalkyl, alkyl, aralkyl, cycloalkyl and aryl, wherein haloalkyl, alkyl, aralkyl, cycloalkyl, and aryl each is independently optionally substituted with one or more radicals selected from the group consisting of alkylthio, nitro and alkylsulfonyl; and

each  $R^4$  is independently selected from the group consisting of hydrido, halo, alkyl, aralkyl, alkoxy, aryloxy, heteroaryloxy, aralkyloxy, heteroaralkyloxy, haloalkyl, haloalkoxy, alkylamino, arylamino, aralkylamino, heteroarylamino, heteroarylalkylamino, nitro, amino, aminosulfonyl, alkylaminosulfonyl, arylaminosulfonyl, heteroarylaminosulfonyl, aralkylaminosulfonyl, heteroaralkylaminosulfonyl, heterocyclosulfonyl, alkylsulfonyl, optionally substituted aryl, optionally substituted heteroaryl, aralkylcarbonyl, heteroarylcarbonyl, arylcarbonyl, aminocarbonyl, and alkylcarbonyl; or wherein  $R^4$  together with ring E forms a naphthyl radical.

12. The method of claim 10, wherein:

n is an integer which is 0, 1, 2, 3 or 4;

G is oxygen or sulfur;

5 R<sup>1</sup> is H;

R<sup>2</sup> is carboxyl, lower alkyl, lower aralkyl or lower alkoxy-carbonyl;

R<sup>3</sup> is lower haloalkyl, lower cycloalkyl or phenyl; and

each R<sup>4</sup> is H, halo, lower alkyl, lower alkoxy, lower haloalkyl, lower haloalkoxy, lower alkylamino, nitro, amino, aminosulfonyl, lower  
 10 alkylaminosulfonyl, 5-membered heteroarylalkylaminosulfonyl, 6-membered heteroarylalkylaminosulfonyl, lower aralkylaminosulfonyl, 5-membered nitrogen-containing heterocyclosulfonyl, 6-membered-nitrogen containing heterocyclosulfonyl, lower alkylsulfonyl, optionally substituted phenyl, lower aralkylcarbonyl, or lower alkylcarbonyl; or

15 wherein R<sup>4</sup> together with the carbon atoms to which it is attached and the remainder of ring E forms a naphthyl radical.

13. The method of claim 10, wherein:

R<sup>2</sup> is carboxyl;

20 R<sup>3</sup> is lower haloalkyl; and

each R<sup>4</sup> is H, halo, lower alkyl, lower haloalkyl, lower haloalkoxy, lower alkylamino, amino, aminosulfonyl, lower alkylaminosulfonyl, 5-membered heteroarylalkylaminosulfonyl, 6-membered heteroarylalkylaminosulfonyl, lower aralkylaminosulfonyl, lower alkylsulfonyl, 6-membered nitrogen-containing  
 25 heterocyclosulfonyl, optionally substituted phenyl, lower aralkylcarbonyl, or lower alkylcarbonyl; or wherein R<sup>4</sup> together with ring E forms a naphthyl radical.

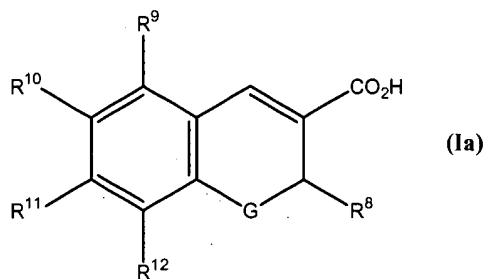
14. The method of claim 10, wherein:

n is an integer which is 0, 1, 2, 3 or 4;

30 R<sup>3</sup> is fluoromethyl, chloromethyl, dichloromethyl, trichloromethyl, pentafluoroethyl, heptafluoropropyl, difluoroethyl, difluoropropyl, dichloroethyl, dichloropropyl, difluoromethyl, or trifluoromethyl; and

each  $R^4$  is H, chloro, fluoro, bromo, iodo, methyl, ethyl, isopropyl, *tert*-butyl, butyl, isobutyl, pentyl, hexyl, methoxy, ethoxy, isopropoxy, *tert*butyloxy, trifluoromethyl, difluoromethyl, trifluoromethoxy, amino, N,N-dimethylamino, N,N-diethylamino, N-phenylmethylaminosulfonyl, N-phenylethylaminosulfonyl, N-(2-furylmethyl)aminosulfonyl, nitro, N,N-dimethylaminosulfonyl, aminosulfonyl, N-methylaminosulfonyl, N-ethylsulfonyl, 2,2-dimethylethylaminosulfonyl, N,N-dimethylaminosulfonyl, N-(2-methylpropyl)aminosulfonyl, N-morpholinosulfonyl, methylsulfonyl, benzylcarbonyl, 2,2-dimethylpropylcarbonyl, phenylacetyl or phenyl; or wherein  $R^4$  together with the carbon atoms to which it is attached and the remainder of ring E forms a naphthyl radical.

15. The method of claim 10 wherein the cyclooxygenase-2 selective inhibitor comprises a compound of the formula:



G is oxygen or sulfur;

15  $R^8$  is trifluoromethyl or pentafluoroethyl;

$R^9$  is H, chloro, or fluoro;

$R^{10}$  is H, chloro, bromo, fluoro, iodo, methyl, *tert*-butyl, trifluoromethoxy, methoxy, benzylcarbonyl, dimethylaminosulfonyl, isopropylaminosulfonyl, methylaminosulfonyl, benzylaminosulfonyl, phenylethylaminosulfonyl, methylpropylaminosulfonyl, methylsulfonyl, or morpholinosulfonyl;

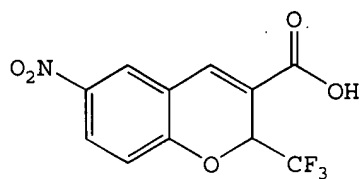
20  $R^{11}$  is H, methyl, ethyl, isopropyl, *tert*-butyl, chloro, methoxy, diethylamino, or phenyl; and

$R^{12}$  is H, chloro, bromo, fluoro, methyl, ethyl, *tert*-butyl, methoxy, or phenyl

16. The method of claim 10 wherein the cyclooxygenase-2 selective inhibitor, pharmaceutically acceptable salt, isomer or prodrug thereof is selected from the group consisting of:
- 6-chloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;
  - 5 6-chloro-7-methyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;
  - 8-(1-methylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;
  - 6-chloro-7-(1,1-dimethylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;
  - 6-chloro-8-(1-methylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;
  - 2-trifluoromethyl-3H-naphthopyran-3-carboxylic acid ;
  - 10 7-(1,1-dimethylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;
  - 6-bromo-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;
  - 8-chloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;
  - 6-trifluoromethoxy-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;
  - 5,7-dichloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;
  - 15 8-phenyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;
  - 7,8-dimethyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;
  - 6,8-bis(dimethylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;
  - 7-(1-methylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;
  - 7-phenyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;
  - 20 6-chloro-7-ethyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;
  - 6-chloro-8-ethyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;
  - 6-chloro-7-phenyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;
  - 6,7-dichloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;
  - 6,8-dichloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;
  - 25 2-trifluoromethyl-3H-naptho[2,1-b]pyran-3-carboxylic acid;
  - 6-chloro-8-methyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;
  - 8-chloro-6-methyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;
  - 8-chloro-6-methoxy-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;
  - 6-bromo-8-chloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;
  - 30 8-bromo-6-fluoro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;
  - 8-bromo-6-methyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;
  - 8-bromo-5-fluoro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

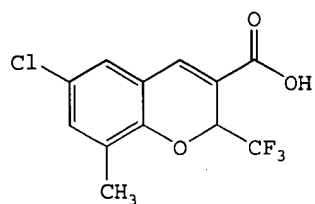
- 6-chloro-8-fluoro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;  
 6-bromo-8-methoxy-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;  
 6-[[[(phenylmethyl)amino]sulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic  
 acid;  
 5 6-[(dimethylamino)sulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;  
 6-[(methylamino)sulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;  
 6-[(4-morpholino)sulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;  
 6-[(1,1-dimethylethyl)aminosulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-  
 carboxylic acid;  
 10 6-[(2-methylpropyl)aminosulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic  
 acid;  
 6-methylsulfonyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;  
 8-chloro-6-[[[(phenylmethyl)amino]sulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-  
 carboxylic acid;  
 15 6-phenylacetyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;  
 6,8-dibromo-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;  
 8-chloro-5,6-dimethyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;  
 6,8-dichloro-(*S*)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;  
 6-benzylsulfonyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;  
 20 6-[[N-(2-furylmethyl)amino]sulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-  
 carboxylic acid;  
 6-[[N-(2-phenylethyl)amino]sulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-  
 carboxylic acid;  
 6-iodo-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;  
 25 7-(1,1-dimethylethyl)-2-pentafluoroethyl-2H-1-benzopyran-3-carboxylic acid; and  
 6-chloro-2-trifluoromethyl-2H-1-benzothiopyran-3-carboxylic acid.

17. The method of claim 10 wherein the cyclooxygenase-2 selective  
 inhibitor, pharmaceutically acceptable salt or prodrug thereof is selected from the  
 30 group consisting of formulas:  
 a)



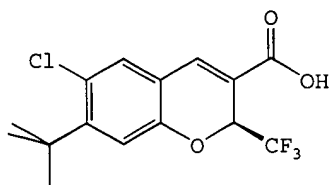
6-Nitro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid

b)



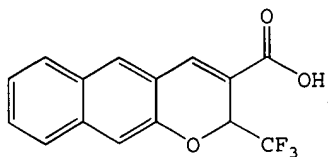
6-Chloro-8-methyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid

c)



((S)-6-Chloro-7-(1,1-dimethylethyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid

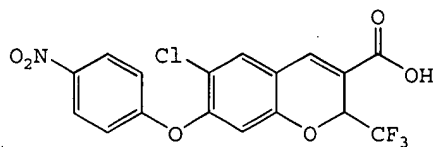
d)



2-Trifluoromethyl-2H-naphtho[2,3-b]pyran-3-carboxylic acid

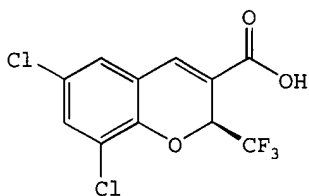


e)



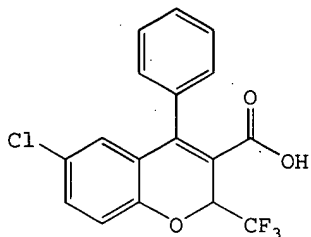
6-Chloro-7-(4-nitrophenoxy)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid

f)



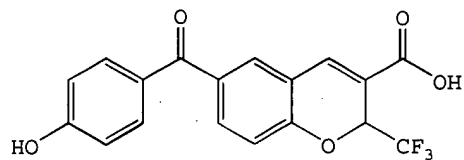
((S))-6,8-Dichloro-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid

g)



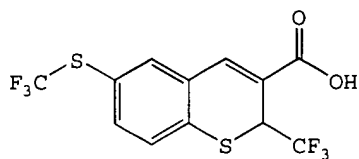
6-Chloro-2-(trifluoromethyl)-4-phenyl-2H-1-benzopyran-3-carboxylic acid

h)



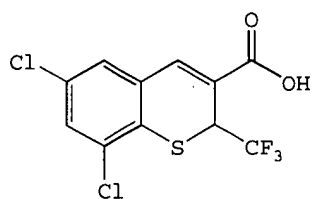
6-(4-Hydroxybenzoyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid

i)



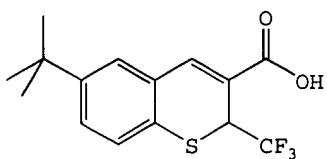
2-(Trifluoromethyl)-6-[(trifluoromethyl)thio]-2H-1-benzothiopyran-3-carboxylic acid

j)



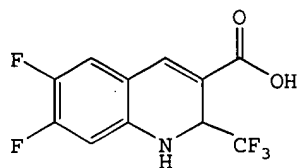
6,8-Dichloro-2-trifluoromethyl-2H-1-benzothiopyran-3-carboxylic acid

k)



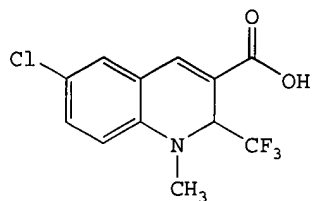
6-(1,1-Dimethylethyl)-2-(trifluoromethyl)-2H-1-benzothiopyran-3-carboxylic acid

l)



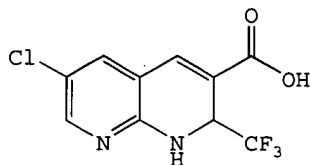
6,7-Difluoro-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid

m)



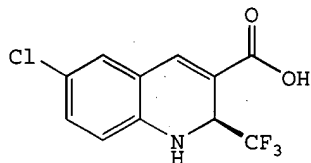
6-Chloro-1,2-dihydro-1-methyl-2-(trifluoromethyl)-3-quinolinecarboxylic acid

n)



6-Chloro-2-(trifluoromethyl)-1,2-dihydro[1,8]naphthyridine-3-carboxylic acid

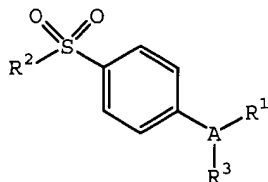
o)



((S)-6-Chloro-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid

and any combination thereof.

18. The method of claim 1 wherein the cyclooxygenase inhibitor comprises a composition of the formula:



wherein A is selected from the group consisting of partially unsaturated or unsaturated heterocyclyl and partially unsaturated or unsaturated carbocyclic rings;

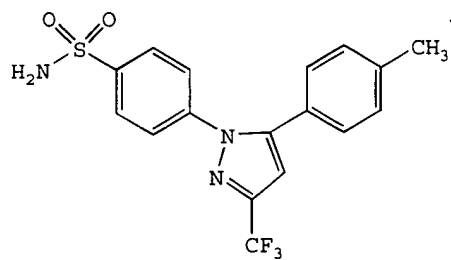
wherein R<sup>1</sup> is selected from the group consisting of heterocyclyl, cycloalkyl, cycloalkenyl and aryl, wherein R<sup>1</sup> is optionally substituted at a substitutable position with one or more radicals selected from alkyl, haloalkyl, cyano, carboxyl, alkoxycarbonyl, hydroxyl, hydroxyalkyl, haloalkoxy, amino, alkylamino, arylamino, nitro, alkoxyalkyl, alkylsulfinyl, halo, alkoxy and alkylthio;

wherein R<sup>2</sup> is selected from the group consisting of methyl or amino; and

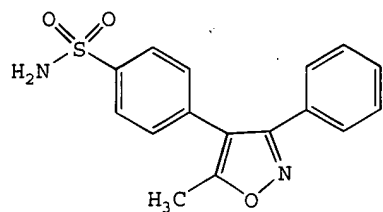
wherein R<sup>3</sup> is selected from the group consisting of a radical selected from H, halo, alkyl, alkenyl, alkynyl, oxo, cyano, carboxyl, cyanoalkyl, heterocycloxy, alkyloxy, alkylthio, alkylcarbonyl, cycloalkyl, aryl, haloalkyl, heterocyclyl, cycloalkenyl, aralkyl, heterocyclylalkyl, acyl, alkylthioalkyl, hydroxyalkyl, alkoxycarbonyl, arylcarbonyl, aralkylcarbonyl, aralkenyl, alkoxyalkyl, arylthioalkyl, aryloxyalkyl, aralkylthioalkyl, aralkoxyalkyl, alkoxyaralkoxyalkyl, alkoxycarbonylalkyl, aminocarbonyl, aminocarbonylalkyl, alkylaminocarbonyl, N-arylaminocarbonyl, N-alkyl-N-arylaminocarbonyl, alkylaminocarbonylalkyl, carboxyalkyl, alkylamino, N-arylamino, N-aralkylamino, N-alkyl-N-aralkylamino, N-alkyl-N-arylamino, aminoalkyl, alkylaminoalkyl, N-arylaminalkyl, N-aralkylaminoalkyl, N-alkyl-N-aralkylaminoalkyl, N-alkyl-N-arylaminalkyl, aryloxy, aralkoxy, arylthio, aralkylthio, alkylsulfinyl, alkylsulfonyl, aminosulfonyl, alkylaminosulfonyl, N-arylaminosulfonyl, arylsulfonyl, N-alkyl-N-arylaminosulfonyl; or a pharmaceutically acceptable salt or prodrug thereof.

19. The method of claim 1 wherein the cyclooxygenase-2 selective inhibitor pharmaceutically acceptable salt or prodrug thereof is selected from the group consisting of:

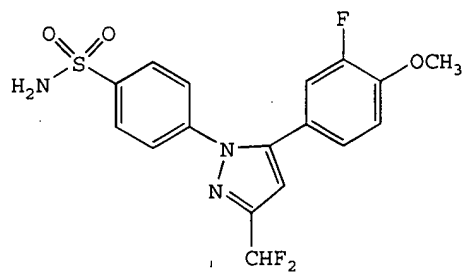
a)



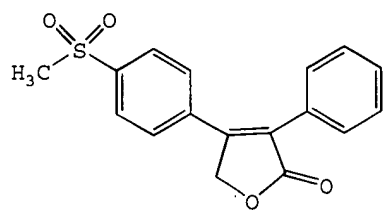
b)



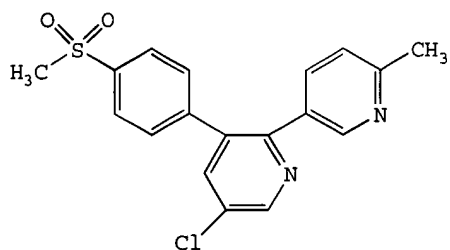
c)



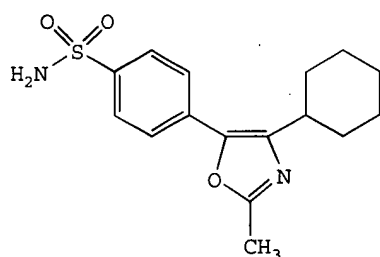
d)



e)



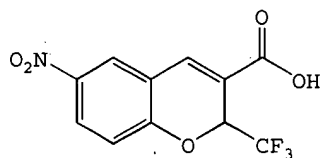
f)



and any combination thereof.

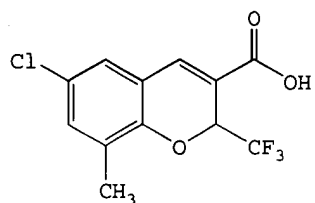
20. The method of claim 1 wherein the cyclooxygenase-2 selective inhibitor or a pharmaceutically acceptable salt or prodrug thereof is selected from the group consisting of:

a)



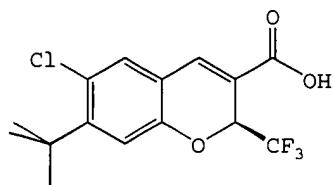
6-Nitro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid

b)



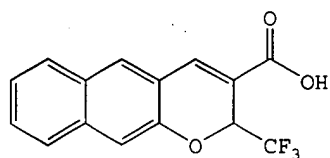
6-Chloro-8-methyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid

c)



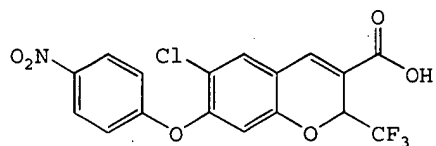
((S)-6-Chloro-7-(1,1-dimethylethyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid

d)



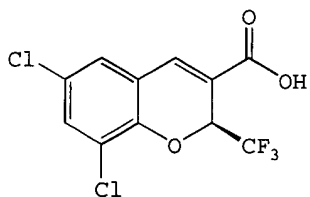
2-Trifluoromethyl-2H-naphtho[2,3-b]pyran-3-carboxylic acid

e)



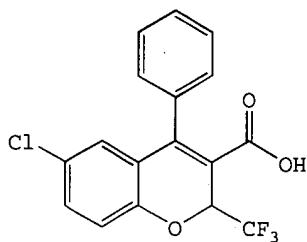
6-Chloro-7-(4-nitrophenoxy)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid

f)



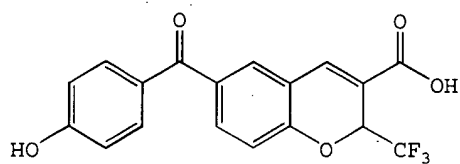
((S)-6,8-Dichloro-2-(trifluoromethyl)-  
2H-1-benzopyran-3-carboxylic acid

g)



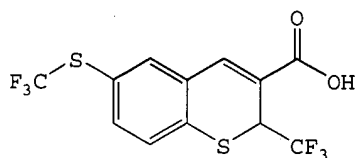
6-Chloro-2-(trifluoromethyl)-4-phenyl-2H-  
1-benzopyran-3-carboxylic acid

h)



6-(4-Hydroxybenzoyl)-2-(trifluoromethyl)-  
2H-1-benzopyran-3-carboxylic acid

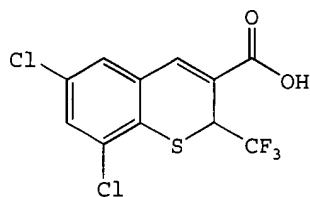
i)



2-(Trifluoromethyl)-6-[(trifluoromethyl)thio]-  
2H-1-benzothiopyran-3-carboxylic acid

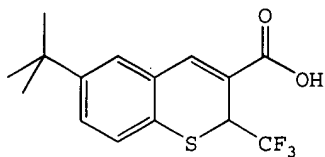


j)



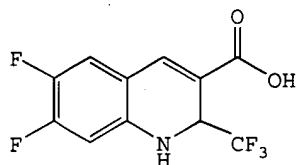
6,8-Dichloro-2-(trifluoromethyl)-2H-1-benzothiopyran-3-carboxylic acid

k)



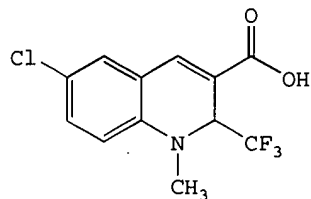
6-(1,1-Dimethylethyl)-2-(trifluoromethyl)-2H-1-benzothiopyran-3-carboxylic acid

l)



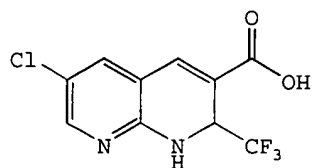
6,7-Difluoro-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid

m)



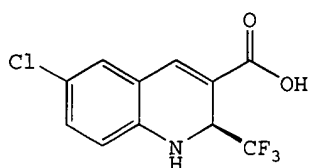
6-Chloro-1,2-dihydro-1-methyl-2-(trifluoromethyl)-3-quinolinecarboxylic acid

n)



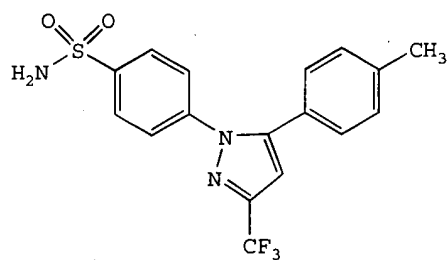
6-Chloro-2-(trifluoromethyl)-1,2-dihydro  
[1,8]naphthyridine-3-carboxylic acid

o)

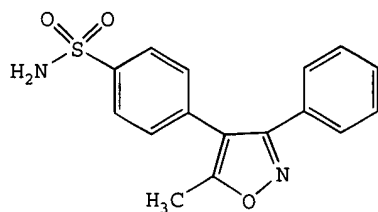


((S)-6-Chloro-1,2-dihydro-2-(trifluoro  
methyl)-3-quinolinecarboxylic acid

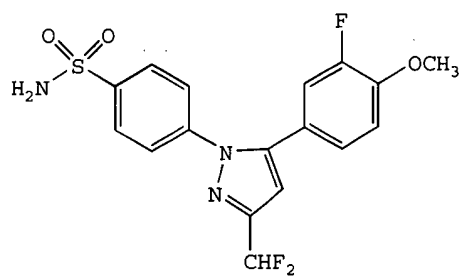
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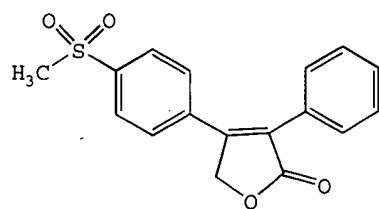
q)



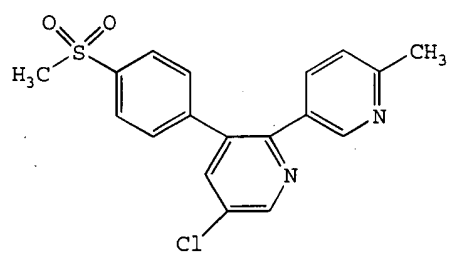
r)



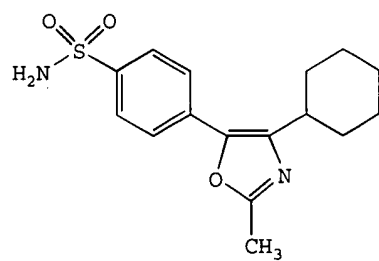
s)



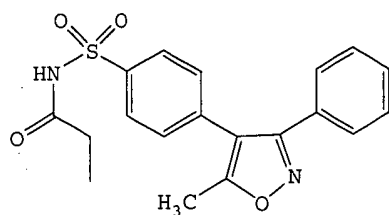
t)



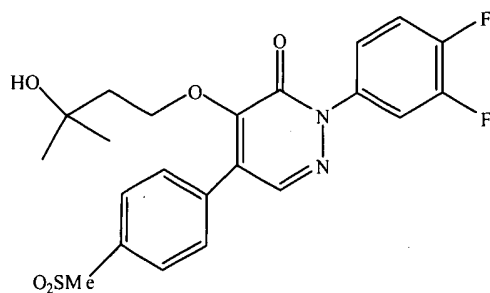
u)



v)

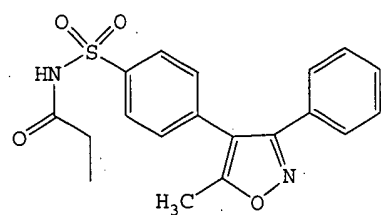


w)



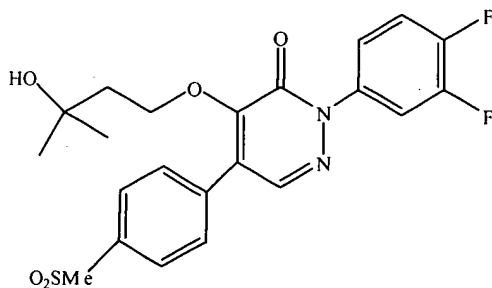
and any combination thereof.

21. The method of claim 1 wherein the cyclooxygenase-2 selective inhibitor  
5 comprises:



or a pharmaceutically acceptable salt or prodrug thereof.

22. The method of claim 1 wherein the cyclooxygenase-2 selective  
10 inhibitor comprises:



or a pharmaceutically acceptable salt or prodrug thereof.

23. The method of claim 1 wherein the cyclooxygenase-2 selective  
5 inhibitor comprises 4-[4-(methyl)-sulfonyl]phenyl]-3-phenyl-2(5H)-furanone, or a  
pharmaceutically acceptable salt or prodrug thereof.

24. The method of claim 1 wherein the cyclooxygenase-2 selective  
inhibitor comprises, 4-(5-methyl-3-phenyl-4-isoxazolyl), or a pharmaceutically  
10 acceptable salt or prodrug thereof.

25. The method of claim 1 wherein the cyclooxygenase-2 selective  
inhibitor comprises, 2-(6-methylpyrid-3-yl)-3-(4-methylsulfonylphenyl)-5-  
chloropyridine, or a pharmaceutically acceptable salt or prodrug thereof.

15

26. The method of claim 1 wherein the cyclooxygenase-2 selective  
inhibitor comprises, 4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl], or a  
pharmaceutically acceptable salt or prodrug thereof.

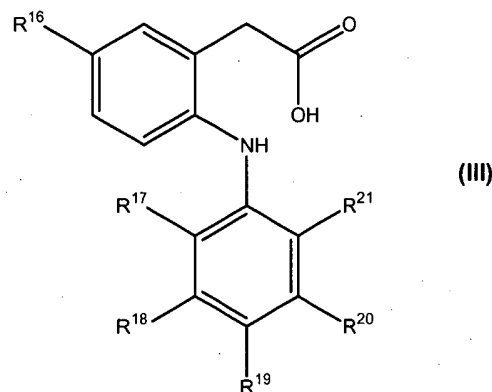
27. The method of claim 1 wherein the cyclooxygenase-2 selective  
20 inhibitor comprises, N-[[4-(5-methyl-3-phenyl-4-isoxazolyl)phenyl]sulfonyl], or a  
pharmaceutically acceptable salt or prodrug thereof.

28. The method of claim 1 wherein the cyclooxygenase-2 selective  
25 inhibitor comprises, 4-[5-(3-fluoro-4-methoxyphenyl)-3-difluoromethyl)-1H-pyrazol-  
1-yl]benzenesulfonamide, or a pharmaceutically acceptable salt or prodrug thereof.

29. The method of claim 1 wherein the cyclooxygenase-2 selective inhibitor comprises, (S)-6,8-dichloro-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid, or a pharmaceutically acceptable salt or prodrug thereof.

5 30. The method of claim 1 wherein the cyclooxygenase-2 selective inhibitor comprises, 2-(3,4-difluorophenyl)-4-(3-hydroxy-3-methylbutoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone, or a pharmaceutically acceptable salt or prodrug thereof.

10 31. The method of claim 1 wherein the cyclooxygenase-2 selective inhibitor comprises a compound of the formula:



wherein:

$R^{16}$  is methyl or ethyl;

$R^{17}$  is chloro or fluoro;

15  $R^{18}$  is hydrogen or fluoro;

$R^{19}$  is hydrogen, fluoro, chloro, methyl, ethyl, methoxy, ethoxy or hydroxy;

$R^{20}$  is hydrogen or fluoro;

$R^{21}$  is chloro, fluoro, trifluoromethyl or methyl,

provided that  $R^{17}$ ,  $R^{18}$ ,  $R^{19}$  and  $R^{20}$  are not all fluoro when  $R^{16}$  is ethyl and  $R^{19}$  is H; or

20 an isomer, a pharmaceutically acceptable salt, ester, or prodrug thereof.

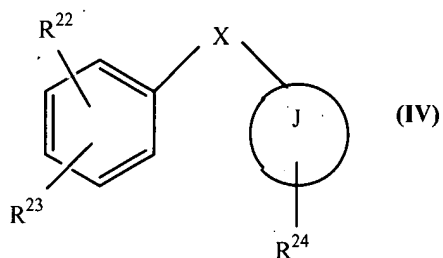
32. The method of claim 31 wherein:

$R^{16}$  is ethyl;

$R^{17}$  and  $R^{19}$  are chloro;

$R^{18}$  and  $R^{20}$  are hydrogen; and  
and  $R^{21}$  is methyl.

33. The method of claim 1 wherein the cyclooxygenase-2 selective  
5 inhibitor comprises a compound of the formula:



wherein:

$X$  is O or S;

$J$  is a carbocycle or a heterocycle;

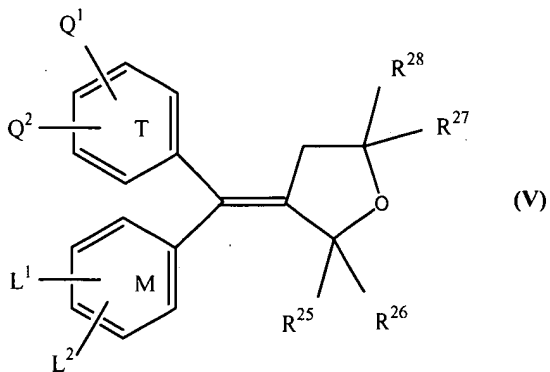
$R^{22}$  is  $\text{NHSO}_2\text{CH}_3$  or F;

10  $R^{23}$  is H,  $\text{NO}_2$ , or F; and

$R^{24}$  is H,  $\text{NHSO}_2\text{CH}_3$ , or  $(\text{SO}_2\text{CH}_3)\text{C}_6\text{H}_4$ ;

or an isomer, a pharmaceutically acceptable salt, an ester, or a prodrug thereof.

34. The method of claim 1 wherein the cyclooxygenase-2 selective  
15 inhibitor comprises a compound of the formula:



wherein:

T and M independently are phenyl, naphthyl, a radical derived from a heterocycle comprising 5 to 6 members and possessing from 1 to 4 heteroatoms, or a radical derived from a saturated hydrocarbon ring having from 3 to 7 carbon atoms;

5      $Q^1$ ,  $Q^2$ ,  $L^1$  or  $L^2$  are independently hydrogen, halogen, lower alkyl having from 1 to 6 carbon atoms, trifluoromethyl, or lower methoxy having from 1 to 6 carbon atoms; and

at least one of  $Q^1$ ,  $Q^2$ ,  $L^1$  or  $L^2$  is in the para position and is  $-S(O)_n-R$ , wherein n is 0, 1, or 2 and R is a lower alkyl radical having 1 to 6 carbon atoms or a lower haloalkyl radical having from 1 to 6 carbon atoms, or an  $-SO_2NH_2$ ; or,

10      $Q^1$  and  $Q^2$  are methylenedioxy; or

$L^1$  and  $L^2$  are methylenedioxy; and

$R^{25}$ ,  $R^{26}$ ,  $R^{27}$ , and  $R^{28}$  are independently hydrogen, halogen, lower alkyl radical having from 1 to 6 carbon atoms, lower haloalkyl radical having from 1 to 6 carbon atoms, or an aromatic radical selected from the group consisting of phenyl, naphthyl, thienyl, furyl and pyridyl; or,

$R^{25}$  and  $R^{26}$  are O; or,

$R^{27}$  and  $R^{28}$  are O; or,

$R^{25}$ ,  $R^{26}$ , together with the carbon atom to which they are attached, form a saturated hydrocarbon ring having from 3 to 7 carbon atoms; or,

20      $R^{27}$ ,  $R^{28}$ , together with the carbon atom to which they are attached, form a saturated hydrocarbon ring having from 3 to 7 carbon atoms;

or an isomer, a pharmaceutically acceptable salt, an ester, or a prodrug thereof.

25     35. The method of claim 1 wherein the cyclooxygenase-2 selective inhibitor, pharmaceutically acceptable salt, isomer, or prodrug thereof is selected from the group consisting of:

3-[(3-Chloro-phenyl)-(4-methanesulfonyl-phenyl)-methylene]-dihydro-furan-2-one;

8-acetyl-3-(4-fluorophenyl)-2-(4-methylsulfonyl)phenyl-imidazo(1,2-a);

30     5,5-dimethyl-4-(4-methylsulfonyl)phenyl-3-phenyl-2-(5H)-furanone ;

5-(4-fluorophenyl)-1-[4-(methylsulfonyl)phenyl]-3-(trifluoromethyl)pyrazole;



- 4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-1-phenyl-3-(trifluoromethyl)pyrazole;
- 4-(5-(4-chlorophenyl)-3-(4-methoxyphenyl)-1H-pyrazol-1-yl)benzenesulfonamide;
- 4-(3,5-bis(4-methylphenyl)-1H-pyrazol-1-yl)benzenesulfonamide;
- 5 4-(5-(4-chlorophenyl)-3-phenyl-1H-pyrazol-1-yl)benzenesulfonamide;
- 4-(3,5-bis(4-methoxyphenyl)-1H-pyrazol-1-yl)benzenesulfonamide;
- 4-(5-(4-chlorophenyl)-3-(4-methylphenyl)-1H-pyrazol-1-yl)benzenesulfonamide;
- 4-(5-(4-chlorophenyl)-3-(4-nitrophenyl)-1H-pyrazol-1-yl)benzenesulfonamide;
- 4-(5-(4-chlorophenyl)-3-(5-chloro-2-thienyl)-1H-pyrazol-1-yl)benzenesulfonamide;
- 10 4-(4-chloro-3,5-diphenyl-1H-pyrazol-1-yl)benzenesulfonamide;
- 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;
- 4-[5-phenyl-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;
- 4-[5-(4-fluorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;
- 4-[5-(4-methoxyphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;
- 15 4-[5-(4-chlorophenyl)-3-(difluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;
- 4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;
- 4-[4-chloro-5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;
- 4-[3-(difluoromethyl)-5-(4-methylphenyl)-1H-pyrazol-1-yl]benzenesulfonamide;
- 20 4-[3-(difluoromethyl)-5-phenyl-1H-pyrazol-1-yl]benzenesulfonamide;
- 4-[3-(difluoromethyl)-5-(4-methoxyphenyl)-1H-pyrazol-1-yl]benzenesulfonamide;
- 4-[3-cyano-5-(4-fluorophenyl)-1H-pyrazol-1-yl]benzenesulfonamide;
- 4-[3-(difluoromethyl)-5-(3-fluoro-4-methoxyphenyl)-1H-pyrazol-1-yl]benzenesulfonamide;
- 25 4-[5-(3-fluoro-4-methoxyphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;
- 4-[4-chloro-5-phenyl-1H-pyrazol-1-yl]benzenesulfonamide;
- 4-[5-(4-chlorophenyl)-3-(hydroxymethyl)-1H-pyrazol-1-yl]benzenesulfonamide;
- 4-[5-(4-(N,N-dimethylamino)phenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;
- 30 5-(4-fluorophenyl)-6-[4-(methylsulfonyl)phenyl]spiro[2.4]hept-5-ene;
- 4-[6-(4-fluorophenyl)spiro[2.4]hept-5-en-5-yl]benzenesulfonamide;

- 6-(4-fluorophenyl)-7-[4-(methylsulfonyl)phenyl]spiro[3.4]oct-6-ene;  
 5-(3-chloro-4-methoxyphenyl)-6-[4-(methylsulfonyl)phenyl]spiro[2.4]hept-5-ene;  
 4-[6-(3-chloro-4-methoxyphenyl)spiro[2.4]hept-5-en-5-yl]benzenesulfonamide;  
 5-(3,5-dichloro-4-methoxyphenyl)-6-[4-(methylsulfonyl)phenyl]spiro[2.4]hept-5-ene;  
 5 5-(3-chloro-4-fluorophenyl)-6-[4-(methylsulfonyl)phenyl]spiro[2.4]hept-5-ene ;  
 4-[6-(3,4-dichlorophenyl)spiro[2.4]hept-5-en-5-yl]benzenesulfonamide;  
 2-(3-chloro-4-fluorophenyl)-4-(4-fluorophenyl)-5-(4-methylsulfonylphenyl)thiazole;  
 2-(2-chlorophenyl)-4-(4-fluorophenyl)-5-(4-methylsulfonylphenyl)thiazole;  
 5-(4-fluorophenyl)-4-(4-methylsulfonylphenyl)-2-methylthiazole;  
 10 4-(4-fluorophenyl)-5-(4-methylsulfonylphenyl)-2-trifluoromethylthiazole;  
 4-(4-fluorophenyl)-5-(4-methylsulfonylphenyl)-2-(2-thienyl)thiazole;  
 4-(4-fluorophenyl)-5-(4-methylsulfonylphenyl)-2-benzylaminothiazole;  
 4-(4-fluorophenyl)-5-(4-methylsulfonylphenyl)-2-(1-propylamino)thiazole;  
 2-[(3,5-dichlorophenoxy)methyl]-4-(4-fluorophenyl)-5-[4-  
 15 (methylsulfonyl)phenyl]thiazole;  
 5-(4-fluorophenyl)-4-(4-methylsulfonylphenyl)-2-trifluoromethylthiazole;  
 1-methylsulfonyl-4-[1,1-dimethyl-4-(4-fluorophenyl)cyclopenta-2,4-dien-3-  
 yl]benzene;  
 4-[4-(4-fluorophenyl)-1,1-dimethylcyclopenta-2,4-dien-3-yl]benzenesulfonamide;  
 20 5-(4-fluorophenyl)-6-[4-(methylsulfonyl)phenyl]spiro[2.4]hepta-4,6-diene;  
 4-[6-(4-fluorophenyl)spiro[2.4]hepta-4,6-dien-5-yl]benzenesulfonamide;  
 6-(4-fluorophenyl)-2-methoxy-5-[4-(methylsulfonyl)phenyl]-pyridine-3-carbonitrile;  
 2-bromo-6-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-pyridine-3-carbonitrile;  
 6-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-2-phenyl-pyridine-3-carbonitrile;  
 25 4-[2-(4-methylpyridin-2-yl)-4-(trifluoromethyl)-1H-imidazol-1-  
 yl]benzenesulfonamide;  
 4-[2-(5-methylpyridin-3-yl)-4-(trifluoromethyl)-1H-imidazol-1-  
 yl]benzenesulfonamide;  
 4-[2-(2-methylpyridin-3-yl)-4-(trifluoromethyl)-1H-imidazol-1-  
 30 yl]benzenesulfonamide;  
 3-[1-[4-(methylsulfonyl)phenyl]-4-(trifluoromethyl)-1H-imidazol-2-yl]pyridine;  
 2-[1-[4-(methylsulfonyl)phenyl]-4-(trifluoromethyl)-1H-imidazol-2-yl]pyridine;

- 2-methyl-4-[1-[4-(methylsulfonyl)phenyl]-4-(trifluoromethyl)-1H-imidazol-2-yl]pyridine;
- 2-methyl-6-[1-[4-(methylsulfonyl)phenyl]-4-(trifluoromethyl)-1H-imidazol-2-yl]pyridine;
- 5 4-[2-(6-methylpyridin-3-yl)-4-(trifluoromethyl)-1H-imidazol-1-yl]benzenesulfonamide;
- 2-(3,4-difluorophenyl)-1-[4-(methylsulfonyl)phenyl]-4-(trifluoromethyl)-1H-imidazole;
- 4-[2-(4-methylphenyl)-4-(trifluoromethyl)-1H-imidazol-1-yl]benzenesulfonamide;
- 10 2-(4-chlorophenyl)-1-[4-(methylsulfonyl)phenyl]-4-methyl-1H-imidazole;
- 2-(4-chlorophenyl)-1-[4-(methylsulfonyl)phenyl]-4-phenyl-1H-imidazole;
- 2-(4-chlorophenyl)-4-(4-fluorophenyl)-1-[4-(methylsulfonyl)phenyl]-1H-imidazole;
- 2-(3-fluoro-4-methoxyphenyl)-1-[4-(methylsulfonyl)phenyl]-4-(trifluoromethyl)-1H-imidazole;
- 15 1-[4-(methylsulfonyl)phenyl]-2-phenyl-4-trifluoromethyl-1H-imidazole;
- 2-(4-methylphenyl)-1-[4-(methylsulfonyl)phenyl]-4-trifluoromethyl-1H-imidazole;
- 4-[2-(3-chloro-4-methylphenyl)-4-(trifluoromethyl)-1H-imidazol-1-yl]benzenesulfonamide;
- 2-(3-fluoro-5-methylphenyl)-1-[4-(methylsulfonyl)phenyl]-4-(trifluoromethyl)-1H-imidazole;
- 20 4-[2-(3-fluoro-5-methylphenyl)-4-(trifluoromethyl)-1H-imidazol-1-yl]benzenesulfonamide;
- 2-(3-methylphenyl)-1-[4-(methylsulfonyl)phenyl]-4-trifluoromethyl-1H-imidazole;
- 4-[2-(3-methylphenyl)-4-trifluoromethyl-1H-imidazol-1-yl]benzenesulfonamide;
- 25 1-[4-(methylsulfonyl)phenyl]-2-(3-chlorophenyl)-4-trifluoromethyl-1H-imidazole;
- 4-[2-(3-chlorophenyl)-4-trifluoromethyl-1H-imidazol-1-yl]benzenesulfonamide;
- 4-[2-phenyl-4-trifluoromethyl-1H-imidazol-1-yl]benzenesulfonamide;
- 4-[2-(4-methoxy-3-chlorophenyl)-4-trifluoromethyl-1H-imidazol-1-yl]benzenesulfonamide;
- 30 1-allyl-4-(4-fluorophenyl)-3-[4-(methylsulfonyl)phenyl]-5-(trifluoromethyl)-1H-pyrazole;

- 4-[1-ethyl-4-(4-fluorophenyl)-5-(trifluoromethyl)-1H-pyrazol-3-yl]benzenesulfonamide;
- N-phenyl-[4-(4-fluorophenyl)-3-[4-(methylsulfonyl)phenyl]-5-(trifluoromethyl)-1H-pyrazol-1-yl]acetamide;
- 5 ethyl [4-(4-fluorophenyl)-3-[4-(methylsulfonyl)phenyl]-5-(trifluoromethyl)-1H-pyrazol-1-yl]acetate;
- 4-(4-fluorophenyl)-3-[4-(methylsulfonyl)phenyl]-1-(2-phenylethyl)-1H-pyrazole;
- 4-(4-fluorophenyl)-3-[4-(methylsulfonyl)phenyl]-1-(2-phenylethyl)-5-(trifluoromethyl)pyrazole;
- 10 1-ethyl-4-(4-fluorophenyl)-3-[4-(methylsulfonyl)phenyl]-5-(trifluoromethyl)-1H-pyrazole;
- 5-(4-fluorophenyl)-4-(4-methylsulfonylphenyl)-2-trifluoromethyl-1H-imidazole;
- 4-[4-(methylsulfonyl)phenyl]-5-(2-thiophenyl)-2-(trifluoromethyl)-1H-imidazole;
- 5-(4-fluorophenyl)-2-methoxy-4-[4-(methylsulfonyl)phenyl]-6-
- 15 (trifluoromethyl)pyridine;
- 2-ethoxy-5-(4-fluorophenyl)-4-[4-(methylsulfonyl)phenyl]-6-(trifluoromethyl)pyridine;
- 5-(4-fluorophenyl)-4-[4-(methylsulfonyl)phenyl]-2-(2-propynyloxy)-6-(trifluoromethyl)pyridine;
- 20 2-bromo-5-(4-fluorophenyl)-4-[4-(methylsulfonyl)phenyl]-6-(trifluoromethyl)pyridine;
- 4-[2-(3-chloro-4-methoxyphenyl)-4,5-difluorophenyl]benzenesulfonamide;
- 1-(4-fluorophenyl)-2-[4-(methylsulfonyl)phenyl]benzene;
- 5-difluoromethyl-4-(4-methylsulfonylphenyl)-3-phenylisoxazole;
- 25 4-[3-ethyl-5-phenylisoxazol-4-yl]benzenesulfonamide;
- 4-[5-difluoromethyl-3-phenylisoxazol-4-yl]benzenesulfonamide;
- 4-[5-hydroxymethyl-3-phenylisoxazol-4-yl]benzenesulfonamide;
- 4-[5-methyl-3-phenyl-isoxazol-4-yl]benzenesulfonamide;
- 1-[2-(4-fluorophenyl)cyclopenten-1-yl]-4-(methylsulfonyl)benzene;
- 30 1-[2-(4-fluoro-2-methylphenyl)cyclopenten-1-yl]-4-(methylsulfonyl)benzene;
- 1-[2-(4-chlorophenyl)cyclopenten-1-yl]-4-(methylsulfonyl)benzene;
- 1-[2-(2,4-dichlorophenyl)cyclopenten-1-yl]-4-(methylsulfonyl)benzene;

- 1-[2-(4-trifluoromethylphenyl)cyclopenten-1-yl]-4-(methylsulfonyl)benzene;  
 1-[2-(4-methylthiophenyl)cyclopenten-1-yl]-4-(methylsulfonyl)benzene;  
 1-[2-(4-fluorophenyl)-4,4-dimethylcyclopenten-1-yl]-4-(methylsulfonyl)benzene;  
 4-[2-(4-fluorophenyl)-4,4-dimethylcyclopenten-1-yl]benzenesulfonamide;  
 5 1-[2-(4-chlorophenyl)-4,4-dimethylcyclopenten-1-yl]-4-(methylsulfonyl)benzene;  
 4-[2-(4-chlorophenyl)-4,4-dimethylcyclopenten-1-yl]benzenesulfonamide;  
 4-[2-(4-fluorophenyl)cyclopenten-1-yl]benzenesulfonamide;  
 4-[2-(4-chlorophenyl)cyclopenten-1-yl]benzenesulfonamide;  
 1-[2-(4-methoxyphenyl)cyclopenten-1-yl]-4-(methylsulfonyl)benzene;  
 10 1-[2-(2,3-difluorophenyl)cyclopenten-1-yl]-4-(methylsulfonyl)benzene;  
 4-[2-(3-fluoro-4-methoxyphenyl)cyclopenten-1-yl]benzenesulfonamide;  
 1-[2-(3-chloro-4-methoxyphenyl)cyclopenten-1-yl]-4-(methylsulfonyl)benzene;  
 4-[2-(3-chloro-4-fluorophenyl)cyclopenten-1-yl]benzenesulfonamide;  
 4-[2-(2-methylpyridin-5-yl)cyclopenten-1-yl]benzenesulfonamide;  
 15 ethyl 2-[4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]oxazol-2-yl]-2-benzyl-  
 acetate;  
 2-[4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]oxazol-2-yl]acetic acid;  
 2-(*tert*-butyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]oxazole;  
 4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-2-phenyloxazole;  
 20 4-(4-fluorophenyl)-2-methyl-5-[4-(methylsulfonyl)phenyl]oxazole;  
 4-[5-(3-fluoro-4-methoxyphenyl)-2-trifluoromethyl-4-oxazolyl]benzenesulfonamide;  
 6-chloro-7-(1,1-dimethylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;  
 6-chloro-8-methyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;  
 5,5-dimethyl-3-(3-fluorophenyl)-4-methylsulfonyl-2(5H)-furanone;  
 25 6-chloro-2-trifluoromethyl-2H-1-benzothiopyran-3-carboxylic acid;  
 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;  
 4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;  
 4-[5-(3-fluoro-4-methoxyphenyl)-3-(difluoromethyl)-1H-pyrazol-1-  
 yl]benzenesulfonamide;  
 30 3-[1-[4-(methylsulfonyl)phenyl]-4-trifluoromethyl-1H-imidazol-2-yl]pyridine;  
 2-methyl-5-[1-[4-(methylsulfonyl)phenyl]-4-trifluoromethyl-1H-imidazol-2-  
 yl]pyridine;

- 4-[2-(5-methylpyridin-3-yl)-4-(trifluoromethyl)-1H-imidazol-1-yl]benzenesulfonamide;
- 4-[5-methyl-3-phenylisoxazol-4-yl]benzenesulfonamide;
- 4-[5-hydroxymethyl-3-phenylisoxazol-4-yl]benzenesulfonamide;
- 5 [2-trifluoromethyl-5-(3,4-difluorophenyl)-4-oxazolyl]benzenesulfonamide;
- 4-[2-methyl-4-phenyl-5-oxazolyl]benzenesulfonamide;
- 4-[5-(2-fluoro-4-methoxyphenyl)-2-trifluoromethyl-4-oxazolyl]benzenesulfonamide;
- [2-(2-chloro-6-fluoro-phenylamino)-5-methyl-phenyl]-acetic acid;
- N-(4-Nitro-2-phenoxy-phenyl)-methanesulfonamide or nimesulide;
- 10 N-[6-(2,4-difluoro-phenoxy)-1-oxo-indan-5-yl]-methanesulfonamide;
- N-[6-(2,4-Difluoro-phenylsulfanyl)-1-oxo-1H-inden-5-yl]-methanesulfonamide, sodium salt;
- N-[5-(4-fluoro-phenylsulfanyl)-thiophen-2-yl]-methanesulfonamide;
- 3-(3,4-Difluoro-phenoxy)-4-(4-methanesulfonyl-phenyl)-5-methyl-5-(2,2,2-trifluoro-ethyl)-5H-furan-2-one;
- 15 (5Z)-2-amino-5-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]methylene]-4(5H)-thiazolone;
- N-[3-(formylamino)-4-oxo-6-phenoxy-4H-1-benzopyran-7-yl]-methanesulfonamide;
- (6aR,10aR)-3-(1,1-dimethylheptyl)-6a,7,10,10a-tetrahydro-1-hydroxy-6,6-dimethyl-6H-dibenzo[b,d]pyran-9-carboxylic acid;
- 20 4-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]methylene]dihydro-2-methyl-2H-1,2-oxazin-3(4H)-one;
- 6-dioxo-9H-purin-8-yl-cinnamic acid;
- 4-[4-(methyl)-sulfonyl]phenyl]-3-phenyl-2(5H)-furanone;
- 25 4-(5-methyl-3-phenyl-4-isoxazolyl);
- 2-(6-methylpyrid-3-yl)-3-(4-methylsulfonylphenyl)-5-chloropyridine;
- 4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl];
- N-[[4-(5-methyl-3-phenyl-4-isoxazolyl)phenyl]sulfonyl];
- 4-[5-(3-fluoro-4-methoxyphenyl)-3-difluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;
- 30 (S)-6,8-dichloro-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

2-(3,4-difluorophenyl)-4-(3-hydroxy-3-methylbutoxy)-5-[4-(methylsulfonyl)phenyl]-  
3(2H)-pyridzainone;  
2-trifluoromethyl-3H-naphtho[2,1-b]pyran-3-carboxylic acid;  
6-chloro-7-(1,1-dimethylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;  
5 and  
[2-(2,4-dichloro-6-ethyl-3,5-dimethyl-phenylamino)-5-propyl-phenyl]-acetic acid.

36. The method of claim 1 wherein the amyloid beta vaccine is a peptide vaccine.

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37. The method of claim 1 wherein the amyloid beta vaccine is a nucleic acid vaccine.

38. The method of claim 36 wherein the amyloid beta vaccine comprises at  
15 least one amyloid beta peptide selected from Abeta (1-43), or a fragment, variant, or analog thereof.

39. The method of claim 38 wherein the amyloid beta peptide is selected from the group consisting of Abeta (1-42), Abeta (1-43), Abeta (1-40), Abeta (1-39),  
20 Abeta (1-41), Abeta (1-28), Abeta (1-16), Abeta (25-35), Abeta (29-39), Abeta(29-40), Abeta (29-41), Abeta (29-42), Abeta (29-43), Abeta (26-42), Abeta (26-43), and Abeta (35-43).

40. The method of claim 39 wherein the amyloid beta peptide is Abeta (1-  
25 42).

41. The method of claim 38 wherein the amyloid beta vaccine further comprises an adjuvant.

30 42. The method of claim 41 wherein the adjuvant is aluminum hydroxide.

43. The method of claim 41 wherein the adjuvant is aluminum phosphate.

44. The method of claim 36 wherein the amyloid beta vaccine is a monovalent vaccine.

5 45. The method of claim 36 wherein the amyloid beta vaccine is a multivalent vaccine.

46. The method of claim 1 wherein the amyloid beta vaccine is administered prior to the administration of the Cox-2 inhibitor.

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47. The method of claim 1 wherein the Cox-2 inhibitor is administered during time intervals between each amyloid beta vaccination.

48. The method of claim 1 wherein the amyloid beta vaccine is  
15 administered following the administration of the Cox-2 inhibitor.

49. The method of claim 1 wherein the amyloid beta vaccine is administered for the life of the subject.

20 50. The method of claim 1 wherein the subject is a mammal.

51. The method of claim 50 wherein the mammal is a human being.

52. A composition comprising an amyloid beta vaccine and a  
25 cyclooxygenase-2 selective inhibitor or a pharmaceutically acceptable salt or prodrug thereof.

53. The composition of claim 52 wherein the cyclooxygenase-2 selective inhibitor comprises a chromene compound.

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54. The composition of claim 53 wherein the chromene compound is a benzopyran or substituted benzopyran analog.



55. The composition of claim 54 wherein the benzopyran or substituted benzopyran analog is selected from the group consisting of benzothiopyrans, dihydroquinolines and dihydronaphthalenes.

5

56. The composition of claim 52 wherein the cyclooxygenase-2 selective inhibitor comprises a tricyclic compound.

57. The composition of claim 56 wherein the tricyclic compound  
10 comprises a benzenesulfonamide or methylsulfonylbenzene.

58. The composition of claim 52 wherein the cyclooxygenase-2 selective inhibitor comprises a phenyl acetic acid derivative.

59. The composition of claim 52 wherein the amyloid beta vaccine is a  
15 peptide vaccine.

60. The composition of claim 52 wherein the amyloid beta vaccine is a  
nucleic acid vaccine.

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61. The composition of claim 59 wherein the amyloid beta vaccine comprises at least one amyloid beta peptide selected from Abeta (1-43), or a fragment, variant, or analog thereof.

62. The composition of claim 61 wherein the amyloid beta peptide is  
25 selected from the group consisting of Abeta (1-42), Abeta (1-43), Abeta (1-40), Abeta (1-39), Abeta (1-41), Abeta (1-28), Abeta (1-16), Abeta (25-35), Abeta (29-39), Abeta (29-40), Abeta (29-41), Abeta (29-42), Abeta (29-43), Abeta (26-42), Abeta (26-43), and Abeta (35-43).

30

63. The composition of claim 62 wherein the amyloid beta peptide is Abeta (1-42).

64. The composition of claim 61 wherein the amyloid beta vaccine further comprises an adjuvant.

5           65. The composition of claim 64 wherein the adjuvant is aluminum hydroxide.

66. The composition of claim 64 wherein the adjuvant is aluminum phosphate.

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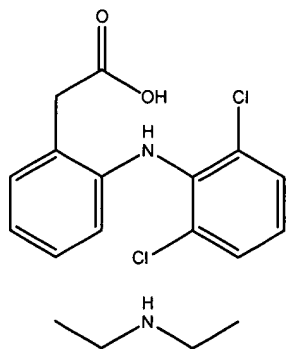
67. The composition of claim 59 wherein the amyloid beta vaccine is a monovalent vaccine.

68. The composition of claim 59 wherein the amyloid beta vaccine is a  
15 multivalent vaccine.

69. The method of claim 1 wherein the vaccine is administered by a route selected from the group consisting of oral, intramuscular, intravenous, subcutaneous, intradermal, and intraperitoneal.

20

70. The method of claim 1 wherein the cyclooxygenase-2 selective inhibitor comprises a compound of the formula:



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